REMARKS

After entry of the present Amendment, claims 94-111, 133, and 136-141 are pending. Claims 94-103, 106, 107, 109, 110, 111, and 137-141 stand rejected under 35 U.S.C. §102(b) as being anticipated by or, in the alternative, under 35 U.S.C §103(a) as being obvious over Smit et al. (*Biochemical and Biophysical Research Communications*, 1992, Vol. 187) (hereinafter "Smit-B"). Claims 94-100, 104-109, 133, 136, 137, 138, 140, and 141 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Smit et al. (Electrophoresis, 1994, Vol. 15, pp. 251-254) (hereinafter "Smit-E") in view of Smit-B and US 4,511,502 ("Bilder"). Applicants respectfully request reconsideration and allowance in view of the remarks herein and the attached Declaration of Inventor Victor Smit.

To clarify the claims, Applicants have amended independent claim 94 to further define that the method for quantitative structure function analysis involves position-specific modification of a molecule. As amended, the claims now define:

- biologically active proteins or peptides having a receptor binding center and a catalytic activity center;
- applying a specific chemical modification of selected amino acids specifically directed to said catalytic activity center of said proteins or said peptides; and
- said modification results in said proteins and said peptides having at least one feature selected from the group consisting of enhanced biological activity, enhanced stability, suppressed antigenicity, acquired antagonistic activity, and cell inhibitory activity and at the same time without distortion of receptor binding activity of said receptor binding center.

Support for this amendment can be found in the specification at least on page 7. Independent claim 110 is also amended.

Applicants respectfully disagree that the cited art discloses or suggests the amended claims, which define position-specific molecule modification. In particular, the cited prior art does not disclose or suggest a method of modifying active proteins or peptides in which a

receptor binding activity of the protein or peptide is not disto ed, but a catalytic activity center of the protein or peptide is modified. In maintaining t rejections, the Office Action suggests:

> The claimed methods comprise modifying amino a ds that are involved in catalytic zinc binding activity. It would have bee obvious to the skilled artisan that a modification of amino acids within pro ins may either result in increased or decreased activity of the protein. It woul have been obvious that modifying zinc binding center of IL-3 to increase zin binding affinity would result in enhanced biological activity, as required by the present claims, because Smit teaches that zinc binding activity f IL-3 is involved in phosphorylation of IL-3 receptor.

Final Office Action of August 7, 2008, p. 3.

However, the generic disclosure of "enhanced biologic activity" by Smit-B does not provide or suggest evidence of position-specific modification which a molecule's catalytic activity is modified without distortion of the binding center o he IL-3 receptor.

As explained by inventor Victor Smit in the attached D laration, cytokines have two distinct centers: (1) a receptor binding center, and (2) a cataly center that performs an action after receptor-binding (Smit Declaration, paragraph 3). As am nded, the claimed method defines that the protein or peptides under analysis have these o distinct centers, and the analysis procedure then specifically targets and then modifies e catalytic center without distortion of the receptor binding center.

It does not follow from the disclosure or "enhanced bi gical activity" by Smit-B referred to by the Office Action that this described enhanced a vity would also lead to modification of the catalytic center, but no changes to the rece r binding center, which leads to superagonism or antoganism. (*Id.* at ¶¶ 8 and 9.) As furthe explained by Mr. Smit in his Declaration, "superagonism" is the modification of a peptide o protein in which receptor binding is not diminished, but catalytic activity is enhanced. (at ¶ 9.) "Antagonism" is modification of a peptide or protein in which receptor binding not diminished, but catalytic activity is significantly diminished or even destroyed. (*Id.* at ¶) In both cases, the catalytic

activity center is modified, but the receptor binding center is not distorted. (*Id.* at ¶¶ 8 and 9.) This situation is also described in the present specification on page 7. Smit-B does not disclose such position-specific modification when this reference refers to enhanced biological activity, and there is no evidence to suggest that such position specific modification is necessarily suggested due to the fact several different positional outcomes may result from modification as explained by Mr. Smit in his declaration. (*See id.* at ¶¶ 4-9.)

In a recent decision by the USPTO Board of Patent Appeals and Interferences, the Board stated that an inherent anticipation and an obviousness rejection need to be supported with specific evidence in the prior art or explained by scientific reasoning to support a conclusion that the claims were anticipated or obvious over the cited art. (*Ex parte Whelan*, 89 USPQ2d 1078, 1083-84 (July 23, 2008). Regarding an inherency rejection, the USPTO Board stated:

> Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient

(*Id.* at 1083.) Regarding obviousness, the USTPTO Appeal board further stated:

> [The Office Action] has not pointed to any teaching in the cited references, or provided any explanation based on scientific reasoning, that would support the conclusion that those skilled in the art would have considered [the claims obvious].

(*Id.* at 1084.) In this case, there is no evidence based on the art of record that describes or even suggests that protein and peptides have two distinct centers—the receptor binding center and the catalytic activity center. Furthermore, there is likewise no evidence in the art of record that also suggests a quantitative structure function analysis that involves position specific modification of the catalytic center without distorting the receptor binding center. The generic disclosure of "enhanced biological activity" does not disclose or suggest, inherently or otherwise, such position specific modification.

Applicants respectfully request entry of the present Amendment, reconsideration and withdrawal of the rejections to claims 94-111, 133, and 136-141 and that the application be passed to issue. The Commissioner is hereby authorized to charge any additional fees which may be required with respect to this communication, or credit any overpayment, to Deposit Account No. 06-1135 regarding 8524/71226.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY

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